Remarks

Amendments to the Claims

Claim 1 is amended to recite a pharmaceutical composition comprising a compound selected from the group shown in Table 1, which specifically alters the binding activity of SR-BI, in combination with a pharmaceutically acceptable carrier. Claim 2 now defines the composition of claim 1, wherein the compound is present in an effective amount to treat a human or animal in need thereof. The phrase wherein the compound is obtained by screening a library of compounds for alteration of SR-B1 binding activity or expression has been deleted in view of the limitation of claim 1 to the actual compounds obtained by screening.

Support for the amendment is found, for example, on page 4, line 15 to page 8, line 22 and page 9, line 26 to page 10, line 18.

Claim 3 is amended to properly recite a Markush group.

Claim 4 has been amended to use the language of claim 1, instead of referring to claim 1.

Claim 10 has been amended to recite the assay methods defined by the claims dependent thereon. The claim has also been amended to refer to a high throughput assay and define the library as a library of small molecules. Support is found at page 2, lines 23-26, and in the examples.

Rejection Under 35 U.S.C. § 112, first paragraph

Claims 1-17 were rejected under 35 U.S.C. § 112, first paragraph, as not being enabled. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

Claim 1 defines a pharmaceutical composition comprising a compound selected from the group shown in Table 1, which specifically alters the binding activity of SR-BI, in combination with a pharmaceutically acceptable carrier.

The 342 compounds in Table 1 were identified by applicants from a library of 16,320 compounds contained in DiverSet E obtained from Chembridge Corporation (page 12, lines 21-23 and page 14, lines 20-23). Chembridge Corp. is a global discovery chemistry contract research organization (CRO) and provider of screening libraries for small molecule drug discovery. The DiverSet is a diverse, pre-designed collection of 10,000 to 50,000 drug-like small molecules. The set is selected based on 3D pharmacophore analysis to cover the broadest part of biologically relevant pharmacophore diversity space (see the attached description from www.chembridge.com). The claims are clearly enabled for the compounds listed in Table 1.

Rejection Under 35 U.S.C. § 112, second paragraph

Claims 1-17 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

Legal Standard

Definiteness of claim language must be analyzed, not in a vacuum, but in light of the content of the particular application disclosure, the teachings of the prior art, and the claim interpretation that would be given by one possessing the ordinary skill in the pertinent art at the time the invention was made. The test for definiteness under 35 U.S.C. 112, second paragraph is whether those skilled in the art would understand what is claimed when the claim is read in light

of the specification. (*Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1576, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986)).

Analysis

Claims 1-9

Claim 1 has been amended to recite a pharmaceutical composition comprising a compound selected from the group shown in Table 1, which specifically alters the binding activity of SR-BI, in combination with a pharmaceutically acceptable carrier. Support for the amendment is found, for example, on page 4, line 15 to page 8, line 22 and page 9, line 26 to page 10, line 18, and from Claim 2.

The Examiner alleges that claim 2 is indefinite because several of the structures in Table 1, which claim 2 references, contain oxygen and nitrogen atoms with open valences, salts which lack negative charges, structures which are not clearly discernable, and/or are duplicates.

Table 1 has been amended to include the hydrogen atoms on oxygen and/or nitrogen which were omitted when the structures were created at the time the application was filed. It is common for those who work in biochemistry, especially with carbon structures, not to include the hydrogen atoms. These have been added so that there is no question as to the claimed structures. Table 1 has also been amended to include positive and/or negative charges where appropriate, to delete duplicate structures, and to correct structures which are difficult to read. Note that the structures in Table 1 have not been renumbered to make it easier for the Examiner to see which structures have been amended or deleted. The applicants are willing to renumber

the structures at the Examiner's request either in a supplemental amendment or in an Examiner's amendment.

The Examiner alleges that claim 3 is indefinite because it refers to a series of compounds without indicating where the compounds are depicted. The limitation in claim 2 that the compound is selected from the group shown in Table 1 has been incorporated into claim 1. Therefore, the Examiner's objection is moot.

Claims 10-17

The Examiner alleges that claim 10 is indefinite as it recites a method of identifying a compound which alters SR-B1 binding activity but merely recites screening a library of compounds without reciting how. Further, the Examiner alleges that dependent claims 11-17 recite limitations which appear to not be part of the method of screening – this is not understood. Should this rejection be maintained, the examiner is asked to please call the undersigned so that an appropriate amendment can be made.

Claim 10 has been amended to define a method of identifying a small molecule compound which alters SR-BI binding activity or expression comprising screening a library of compounds using a high throughput assay for alteration of HDL binding, lipid mediated transport or expression.

Claim 11 defines one type of assay which can be used to determine expression (i.e. Northern blot analysis). Claim 12 defines the type of library which can be screened. Claims 13-17 define the method of claim 10 wherein the assay measures the **inhibition** of SR-B1 activity.

One of ordinary skill in the art would understand what is claimed when the claims are read in light of the specification. Therefore, the claims, as amended, are definite.

Rejection Under 35 U.S.C. § 102

Claim 2 was rejected under 35 U.S.C. § 102(b) as anticipated by Fluorochem and/or Synchem OHG. Claims 1 and 4-17 were rejected under 35 U.S.C. 102(b) as anticipated by U.S. Patent Application Publication No. 2002/0099040 to Krieger *et al.* ("Krieger"); U.S. Patent Application Publication No. 2002/0016364 to Luchoomun *et al.* ("Luchoomun"); and U.S. Patent No. 5,965,790 to Acton *et al.* ("Acton"). Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

The Legal Standard

For a rejection of claims to be properly founded under 35 U.S.C. § 102, it must be established that a prior art reference discloses each and every element of the claims. *Hybritech Inc. v Monoclonal Antibodies Inc.*, 231 USPQ 81 (Fed. Cir. 1986), cert. denied, 480 US 947 (1987); *Scripps Clinic & Research Found v. Genentech Inc.*, 18 USPQ2d 1001 (Fed. Cir. 1991). The Federal Circuit held in *Scripps*, 18 USPQ2d at 1010:

> Invalidity for anticipation requires that all of the elements and limitations of the claim are found within a single prior art reference. . . There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention. (Emphasis added)

A reference that fails to disclose even one limitation will not be found to anticipate, even if the missing limitation could be discoverable through further experimentation. As the Federal Circuit held in Scripps, Id.:

> [A] finding of anticipation requires that all aspects of the claimed invention were already described in a single reference: a finding that is not supportable if it is necessary to prove facts beyond those disclosed in the reference in order to meet the claim limitations. The role of extrinsic evidence is to educate the decision-maker to what the reference meant to persons of ordinary skill in the field of the invention, not to fill in the gaps in the reference.

For a prior art reference to anticipate a claim, it must enable a person skilled in the art to practice the invention. The Federal Circuit held that "a §102(b) reference must sufficiently describe the claimed invention to have placed the public in possession of it. . . [E]ven if the claimed invention is disclosed in a printed publication, that disclosure will not suffice as prior art if it was not enabling." *Paperless Accounting Inc v Bay Area Rapid Transit Sys.*, 231 USPQ 649, 653 (Fed. Cir. 1986).

Analysis

Claim 1 defines a pharmaceutical composition comprising a compound selected from the group shown in Table 1, which specifically alters the binding activity of SR-BI, in combination with a pharmaceutically acceptable carrier.

Claim 4 defines a method for altering cholesterol transport into or out of cells comprising inhibiting expression or activity of SR-BI comprising administering to an animal or human in

need thereof a pharmaceutical composition comprising a compound selected from the group shown in Table 1, which specifically alters the binding activity of SR-BI, in combination with a pharmaceutically acceptable carrier.

Claim 10 defines a method of identifying a small molecule compound which alters SR-BI binding activity or expression comprising screening a library of compounds using a high throughput assay for alteration of HDL binding, lipid mediated transport or expression.

Fluorochem and Synchem

Fluorochem and Synchem are chemical supply companies which supply two of the compounds listed in Table 1. Fluorochem and Synchem do not disclose a pharmaceutical composition comprising a compound selected from the group shown in Table 1, which specifically alters the binding activity of SR-BI, in combination with a pharmaceutically acceptable carrier. Therefore, the claims, as amended, are novel over Fluorochem and Synchem.

Krieger

Krieger was published on July 25, 2002. The applicants' priority date is October 8, 2002. Therefore, Krieger is not available as prior art under 35 U.S.C. § 102(b). At most, Krieger is only available as prior art under 35 U.S.C. § 102(a) or § 102(e).

Claims 1-9

Krieger describes methods for regulation of cholesterol transport based on the regulation of the expression or function of the SR-B1 HDL receptor (paragraph 0017). Direct inhibitors include nucleotide molecules such as antisense oligonucleotides, ribozymes, and triplex forming oligonucleotides which bind to the SR-B1 gene (paragraph 0029). Libraries of known compounds, including natural products or synthetic chemicals, and biologically active materials, including proteins, can be screened for compounds which are inhibitors or activators (paragraph 0069). Krieger, however, does not disclose a pharmaceutical composition comprising a compound *selected from the group shown in Table 1*, which specifically alters the binding activity of SR-BI, in combination with a pharmaceutically acceptable carrier. Krieger does not disclose any of the compounds listed in Table 1 nor does Krieger disclose a method for altering cholesterol transport into or out of cells comprising inhibiting expression or activity of SR-BI comprising administering to an animal or human in need thereof a pharmaceutical composition comprising a compound selected from the group shown in Table 1. Therefore, claims 1-9, as amended, are novel over Krieger.

Claims 10-17

Krieger does not disclose either a high throughput assay nor a library of small molecule inhibitors, as defined by amended claims 10-17. Therefore, claims 10-17, as amended, are novel over Krieger.

Luchoomun

Luchoomun was published on February 7, 2002, which is less than one year before the Applicant's priority date. Luchoomun is not available as prior art under 35 U.S.C. § 102 (b). At most, Luchoomun is only available under 35 U.S.C. § 102 (a) or § 102 (e).

Claims 1-9

Luchoomun describes selected ethers of probucol and their pharmaceutically acceptable salts which are useful for increasing HDL cholesterol. Luchoomun does not disclose a pharmaceutical composition comprising a compound *selected from the group shown in Table 1*, which specifically alters the binding activity of SR-BI, in combination with a pharmaceutically acceptable carrier. Luchoomun does not disclose any of the compounds listed in Table 1 nor does Luchoomun disclose a method for altering cholesterol transport into or out of cells comprising inhibiting expression or activity of SR-BI comprising administering to an animal or human in need thereof a pharmaceutical composition comprising a compound selected from the group shown in Table 1. Therefore, claims 1-9, as amended, are novel over Luchoomun.

Claims 10-17

Luchoomun does not disclose either a high throughput assay nor a library of small molecule inhibitors, as defined by amended claims 10-17. Therefore, claims 10-17, as amended, are novel over Luchoomun.

Acton

Claims 1-9

Acton discloses nucleic acid sequences that can activate or regulate transcription of SR-B1 receptors (col. 1, line 65 to col. 2, line 2). Acton does not disclose a pharmaceutical composition comprising a compound *selected from the group shown in Table 1*, which specifically alters the binding activity of SR-BI, in combination with a pharmaceutically acceptable carrier. Acton does not disclose any of the compounds listed in Table 1 nor does Acton disclose a method for altering cholesterol transport into or out of cells comprising inhibiting expression or activity of SR-BI comprising administering to an animal or human in need thereof a pharmaceutical composition comprising a compound selected from the group shown in Table 1. Therefore, claims 1-9, as amended, are novel over Acton.

Claims 10-17

Acton does not disclose either a high throughput assay nor a library of small molecule inhibitors, as defined by amended claims 10-17. Therefore, claims 10-17, as amended, are novel over Acton.

Rejection Under 35 U.S.C. § 103

Claims 1 and 4-17 were rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent Application Publication No. 2002/0099040 to Krieger ("Krieger") and U.S. Patent No. 5,965,790 to Acton ("Acton"). Claims 13-21 were rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent Application Publication No. 2002/0016364 to Luchoomun *et*

al. ("Luchoomun"). Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

The Legal Standard

To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

"There are three possible sources for a motivation to combine references: the nature of the problem to be solved, the teachings of the prior art, and the knowledge of persons of ordinary skill in the art." *In re Rouffet*, 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1457-58 (Fed. Cir. 1998) (The combination of the references taught every element of the claimed invention, however without a motivation to combine, a rejection based on a prima facie case of obvious was held improper.). The level of skill in the art cannot be relied upon to provide the suggestion to combine references. *Al-Site Corp. v. VSI Int'l Inc.*, 174 F.3d 1308, 50 USPQ2d 1161 (Fed. Cir. 1999).

To establish prima facie obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA

1974). "All words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970). If an independent claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988).

Analysis

Claim 1 defines a pharmaceutical composition comprising a compound selected from the group shown in Table 1, which specifically alters the binding activity of SR-BI, in combination with a pharmaceutically acceptable carrier, wherein the compound is present in an effective amount to treat a human or animal in need thereof, and wherein the compound is obtained by screening a library of compounds for alteration of SR-B1 binding activity or expression.

Claim 4 defines a method for altering cholesterol transport into or out of cells comprising inhibiting expression or activity of SR-BI comprising administering to an animal or human in need thereof a pharmaceutical composition comprising a compound selected from the group shown in Table 1, which specifically alters the binding activity of SR-BI, in combination with a pharmaceutically acceptable carrier.

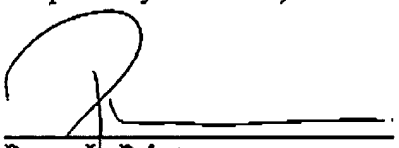
Claim 10 defines a method of identifying a small molecule compound which alters SR-BI binding activity or expression comprising screening a library of compounds using a high throughput assay for alteration of HDL binding, lipid mediated transport or expression.

As discussed above, none of the references disclose or suggest a pharmaceutical composition comprising a compound selected from the group shown in Table 1 as defined by claims 1-3. None of the references disclose or suggest a method for altering cholesterol transport

into or out of cells comprising inhibiting expression or activity of SR-BI comprising administering to an animal or human in need thereof a pharmaceutical composition comprising a compound selected from the group shown in Table 1 as defined in claims 4-9. Finally, none of the references disclose or suggest either a high throughput assay nor a library of small molecule inhibitors, as defined by amended claims 10-17. Therefore, the claims, as amended, are not obvious over Krieger, Luchoomun, and Acton.

Allowance of claims 1-17 is respectfully solicited.

Respectfully submitted,



Patrea L. Pabst
Reg. No. 31,284

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PABST PATENT GROUP LLP
400 Colony Square, Suite 1200
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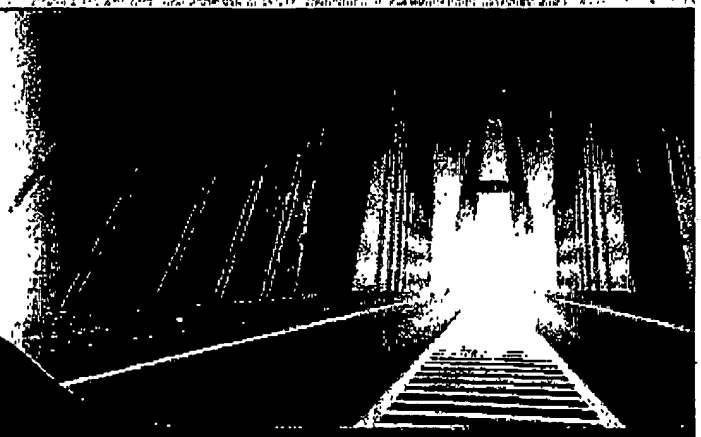

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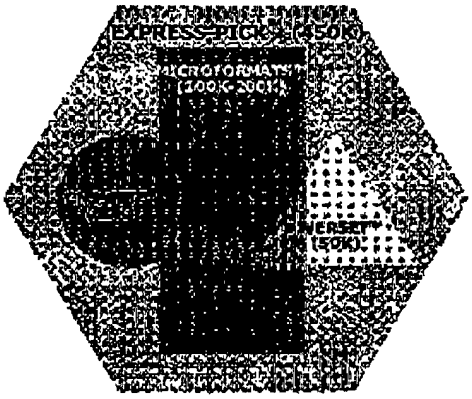

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